#3

DECLARATION

Sir,

I, Stig Steen, declare as follows:

1. I am currently Professor of Cardiothoracic Surgery at the University of Lund. A survey of my medical experience and scientific articles produced by me is presented in the Curriculum Vitae enclosed.
2. Since 1980 I have been involved in research concerning preservation and transplantation of organs and tissues and...
3. I am the inventor behind the invention "improved preservation solution" in the present U.S. continuation-in-part (CIP) application, based on the U.S. patent application No. 08/093,614.
4. I have studied and am familiar with the patent applications mentioned under item 3, and also the references cited in the Office Action issued on 13 November 1998 in the U.S. patent application No. 08/093,614, particularly:

   J.H. Nozick et al. (Autogenous vein graft thrombosis following exposure to calcium-free solutions (calcium paradox), J. Cardiovasc. Surg., 22, 1981)
   Joshizumi Naka et al. (Nitroglycerin maintains graft vascular homeostasis., the Journal of thoracic and cardiovascular surgery, vol. 109, No. 2)
   Kouishi Hisatomi et al. (Beneficial effect of the addition of nitroglycerine... (Japanese Circulation Journal, vol. 57, June 1993))
5. The purpose of the present Declaration is mainly to
   - discuss the important differences between preservation solutions and extracellular solutions, i.e. irrigation/wash/infusion solutions, for organs and tissues,
   - explain the background why since a long time it has been a widespread general knowledge among the skilled in the art that the presence of calcium in preservation solutions would give detrimental effects on the organs and tissues to be preserved before transplantation,
   - explain why a skilled in the art, being aware of the problem to solve according to the present invention and having access to the above-mentioned references cited, would not find any incentive to combine features from these references, thereby arriving at the present invention, and particularly why the calcium presence feature in the Nozick reference can or would not be adopted by the skilled in the art in this context.

   These three main questions are discussed under item 6 below.
6. <u>Extracellular solutions</u>

Extracellular solutions, in the literature sometimes misleadingly called preservation solutions, are solutions having ionic concentrations similar to plasma. The classic extracellular solution is Ringer's solution which has a normal extracellular concentration of sodium, potassium, calcium and magnesium. To match the positive ions for obtaining ionic equivalence, chloride, lactate or acetate are used in different types of Ringer's solution. For

functional in vitro studies the classical organ bath solution is Krebs solution which is electrolytically constructed like Ringer's solution. However, Krebs solution also contains glucose for metabolism and it contains phosphate and bicarbonate buffers to achieve a pH of 7.40 when this solution is bubbled with a mixture of 95 % oxygen and 5 % CO_2 at 37°C. If a cold perfusion is preferred, enough oxygen is physically dissolved to match the lowered metabolism caused by the cooling. However, neither of these two methods have been a success for extended preservation periods in experimental transplantation. During hypothermia rigidity develops in the cell endothelial membranes. This occurs because the fluidity of the lipids is diminished as an effect of the temperature reduction. The rigidity of the endothelium contributes to the endothelial injury described following prolonged cold perfusion with the intention to preserve e.g. the kidney (1-3) and the liver (4).

The calcium paradox

If an organ is perfused with an extracellular solution without calcium for a while and then the perfusion continues with the same solution but now including calcium, the organ may be destroyed quicker compared to perfusing it only with the calcium free solution, i.e. perfusion without calcium is dangerous and perfusion with calcium is dangerous – that is the paradox. In clinical organ preservation the organ is immediately cooled down by flushing it with a cold preservation solution created for e.g. cold anaerobic storage. The composition of preservation solutions used for cold anaerobic storage needs to be constructed in quite another way than extracellular solutions. The calcium paradox has been described as a problem only during aerobic conditions.

Why an organ or tissue preservation solution created for cold anaerobic storage needs to be constructed differently from extracellular solutions used for organ perfusion.

Effects of hypothermia

In the first successful liver transplantation performed, Welch found that 33 minutes of warm ischemia of the dog liver was the upper limit, if the recipient animal was going to survive the operation (5). With this approach, success was noted in 21 of the 49 cases, which survived for at least 5 days. Moore et al., were the first to describe the use of hypothermia in preservation of the liver, namely by surface cooling of the organ, but they did not attempt to prolong the ischemie time to more than half an hour (6). In addition to cooling the whole donor animal by immersing it in an ice-bath, Starzl also used so-called core cooling of the liver by flushing out the blood through the portal vein with chilled Ringer's lactate solution (7, 8). He thereby found that cold ischemic times for up to 2 hours were compatible with survival of the recipient dog, but longer ischemic times resulted in a so-called venous outflow block, leading to the death of the recipient.

It was apparent from these and subsequent studies that hypothermia had a protective effect during ischemia, and in fact, hypothermia has become the main principle in organ preservation. For example, Calne and Pegg showed that simple cooling of ischemic kidneys with cold blood was effective for preserving the function for 12 hours (9). By investigating recipients of paired cadaver kidneys subjected to up to 1 hour of warm ischemia, followed by up to 10 hours of cold ischemia, Bergentz et al. showed that the function was immediate after transplantation of these kidneys (10).

Hypothermia probably exerts its protective effect during ischemia by reducing the rate of cellular metabolism. The reduction in the activity of most enzymes in normothermic animals is approximately 12- to 13-fold when the temperature is reduced from 37°C to close to 0°C (11). Most organs can tolerate a warm ischemic period for 30 to 60 minutes without loss of function. Thus, it could be predicted that simple cooling of the organ could prolong the tolerance of an organ to ischemia to 6-12 hours, which in the case of the kidney is in accordance with the findings of Calne and Pegg (9) and for the lungs with the findings of (12). Thus, cell metabolism decreases during hypothermia, and the consumption of oxygen is reduced. For example, at 5°C, the oxygen consumption in the kidney is only about 5 % of the value at normothermia (13).

Negative effects of hypothermia resulting in the need for special preservation solutions for cold anaerobic storage

Hypothermia per se has certain side-effects. One side-effect is an inhibition of the Na/K ATPase causing a pronounced cell swelling during hypothermia, (14, 15). In fact, since the sodium pump becomes inoperative because of the cooling, swelling will occur even if sufficient ATP is present. The same degree of swelling that occurs in tissue slices incubated at 0°C, can be provoked by incubation with ouabain, an inhibitor of Na/K ATPase (16). Hypothermia induced cell swelling is more prominent in the heart and liver than in the kidney, because of a difference in cold-sensitivity of the membrane pumps between these tissues (15). Similar to the situation during warm ischemia, there will be a cellular loss of potassium and a gain of sodium and calcium as an effect of the inhibition of the membrane pumps.

Calcium dependent cell injury

During normal resting conditions, the intracellular Ca^{2+} concentration is 1000 – 10000 times lower than that of the extracellular fluid (17). This large gradient is maintained by the action of the Ca^{2+}-sequestering system in the mitochondria and endoplasmic reticulum as well as by the action of the Na/Ca-ATPases of the endoplasmic reticulum and the cell membranes (18). Thus, lack of ATP will lead to an increase in the cytoplasmic concentration of Ca^{2+}. Based on the finding that Ca^{2+} accumulates in liver cells damaged by either ischemia or different hepatotoxins (10, 18-21), Farber has suggested that inflow of Ca^{2+} from the extracellular fluid is a final common pathway in liver cell death (21, 23-25). It has also been shown that blockers of Ca^{2+} entry will alleviate liver cell injury (23, 26, 27, 28, 29). Also, calcium ionophors, i.e. compounds that facilitates Ca^{2+} entry across cell membranes, have been shown to cause liver cell death (30). Thus, organ and tissue preservation solutions created for cold anaerobic storage have always been constructed without Ca^{2+}.

As earlier mentioned Starzl used cold Ringer's lactate solution, i.e. not a genuine preservation solution, to flush the liver to obtain core cooling quickly, and this allowed for 2 hours preservation in the dog liver transplantation model (7, 8). Because of the relative inefficiency of this technique, research for several years focused on other methods for organ preservation.

However, in 1969 there was a breakthrough for preservation by simple cold storage. Collins showed that simple cold storage of the kidney for 30 hours was possible with a new type of hypertonic flush-out solution, hereafter named Collins solution (31). This solution

came in immediate use for clinical kidney preservation, and soon became the most used solution worldwide. This solution was calcium free, and had intracellular concentrations of sodium and potassium, i.e. low-sodium and high-potassium concentrations.

In 1977, Collins solution was tried for preservation of the liver, and it allowed 18 hours of preservation of the canine liver (32). This solution was then adopted by Starzl's group for clinical liver preservation (32, 33) and was slightly modified to what is called Eurocollins solution (34) and became the most extensively used liver and kidney preservation solution until the development of the University of Wisconsin preservation solution. Since the extracellular solution Ringer's lactate allows only 2 hours and the intracellular solution Collins solution allows up to 18 hours of cold storage of the canine liver (8, 13), it was obvious that the composition of the cold storage solution influences the results of preservation during cold anaerobic storage. Initially most authors regarded the success behind Collins solution as a result of its high content of potassium (35-37). It was assumed that the intracellular composition of this solution was saving high energy phosphate by decreasing the load of the cell membrane pumps (36). In the early studies it was also assumed that the high content of magnesium was important for the results obtained with Collins solution, presumably by preventing the loss of potassium (35, 36). For that reason Collins solution had a high magnesium content.

However, the role of magnesium was later questioned by other authors, obtaining equally good or even better results with solutions with a low or no content of magnesium (37-39), and in a tissue slice model it was shown that the presence of Mg^{2+} did not influence the loss of K^+ during hypothermia (38). For that reason magnesium was taken away in Eurocollins solution which then was free from both calcium and magnesium. Then the attention was focused on the content of cell membrane impermeant solutes in Collins solution. Collins solution has a high content of glucose and sulfate, which are relatively impermeable in kidney cells. By balancing the osmotic pressure created by the intracellular cell membrane impermeable anions with cell membrane impermeable substances in the preservation solution, the development of hypothermia induced cell swelling during cold storage of the kidneys could be prevented.

Glucose is relatively impermeable to kidney cells but not to liver cells. The high content of glucose in Collins and Eurocollins solution effectively prevents the hypothermia induced cell edema in kidneys, but not in livers. For liver preservation, another solution, named University of Wisconsin solution, glucose was taken away and instead raffinose and lactobionate were added. These two substances are also impermeable to cell membranes both in kidneys and livers. Now 24 hours preservation of the canine liver could be obtained (40, 41). Since 1988 University of Wisconsin solution has been the organ and tissue preservation solution most used in clinical transplantation. University of Wisconsin solution is free of calcium and has an intracellular electrolyte composition. It contains raffinose and lactobionate as cell membrane impermeable molecules to counteract the cold induced cell swelling, and it contains hydroxyetyl-starch to create colloid osmotic pressure.

Extracellular solution versus organ preservation solution created for cold ischemic anaerobic storage

To sum up, it is of the utmost importance to know the difference between on the one hand an extracellular solution which is created for intravenous infusions of a dehydrated patient, and which is also used to irrigate and rinse tissues and wounds, and on the other hand an organ and tissue preservation solution created for cold ischemic storage. As stated above, University of Wisconsin organ preservation solution is today the leading organ preservation solution used for clinical transplantation in the world. To preserve kidneys, livers and pancreas it is almost exclusively used by all transplant surgeons and it is even more and more used in heart preservation. For lung preservation the most used solution has been, and probably still is, Eurocollins solution. Both these solutions are calcium free for the reason earlier discussed. They have intracellular electrolyte compositions and they have cell impermeable molecules and are buffered.

Comments on the article of Nozick: Autogenous Vein Graft Thrombosis Following Exposure to Calcium Free Solutions (calcium paradox)

This article was published in 1981. Nozick used an extracellular solution to irrigate and rinse external jugular veins in dogs before they were autotransplanted into the femoral artery. The veins were irrigated and kept in the extracellular solution for 45 minutes before transplantation. In one group the irrigation solution contained calcium and another was without calcium. It was concluded that it was better to irrigate the veins with extracellular solution containing calcium. However, this study has nothing to do with organ preservation where cold ischemic storage for hours is the aim. When Starzl tried to use Ringer's lactate which also contains calcium, he was not able to preserve canine livers for more than 2 hours. All the researchers making efforts to develop an organ preservation solution in the 80's, i.e. at the same time as Nozick published his article, knew that an organ had to be preserved by quite other principles than simply using extracellular solutions containing calcium. At that time it was a dogma, which not were changed by the publication of the Nozick reference, that an organ preservation solution should be free of calcium so that when the sodium potassium pump stopped due to the hypothermia no extracellular calcium could diffuse into the cells causing cell destruction. Further, Nozick et al. only have performed morphological studies, i.e. electron microscopic studies of the endothel anatomy, but no functional studies of the endothel, more precisely no studies of endothel dependent and independent relaxation, respectively, and also of the calcium influence on contraction and relaxation of the vascular smooth muscles.

The result of the morphological study by Nozick et al. can in no way be correlated to the functional study by the present inventors, and it can not be concluded from the Nozick et al. study that the function of the endothel and smooth muscles is influenced by calcium in such an advantageous manner as found by the present inventors.

Thus, skilled in the art would not take the risk of adapting the results from Nozick et al. with a view to preparing an organ and tissue preservation solution according to the present invention.

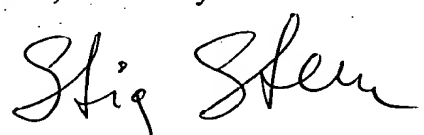
Nitroglycerin in organ preservation solutions

None of the references under item 4 advocates nitroglycerin in organ preservation solutions. The studies where nitroglycerin has been suggested to be of value have been in models where extracellular solutions have been used in lung preservation, (Ringer's solution). In these models, where the endothelium has been injured by cold Ringer's solution, positive effects of nitroglycerin were seen.

7. To conclude, none of the cited references concern organ and tissue preservation solutions in their strict meaning, but only extracellular solutions serving a completely different purpose. Furthermore, the functional effects on the organs and tissues when using the improved preservation solution according to the present invention are by no means derivable or foreseeable from any of the references cited. The calcium present in an extracellular solution in the Nozick reference has only shown a positive structural effect on the endothel of a blood vessel. However, completely different mechanisms are involved in the case of the functional effects, and Nozick is unaware of a completely silent about such functional effects. Also, due to common knowledge regarding the danger of the presence of calcium in preservation solutions, a person skilled in the art would definitely avoid using calcium in preservation solutions.

   Thus, even if a person skilled in the art would consider the content of the references cited in combination, there would still be a gap (inventive step) up to the present invention which by no means would be filled by a person skilled in the art.
8. I hereby declare that all statements made herein of my own knowledge are true and that all statements were made with the knowledge that willful false statements and the like so made of are punishable by fine or imprisonment, or both, under section 1001 of title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Lund, 14 January 2000



Stig Steen
Professor

CURRICULUM VITAE

Personal data

Name	Stig Joar Steen
Date of birth	1948-02-07
Place of birth	Tynset, Norway
Citizenship	Norwegian
Medical School, University of Bergen, Norway	1968-1974
Medical Degree	1976
Speciality qualifications: General surgery	1981
Cardiothoracic surgery	1988
PhD: "Human Vascular α-Adrenoceptors", awarded the Professor Petrén prize	1984
Associate Professor of Surgery, University of Lund, Sweden, since	1987
Declared competent to be Professor in Experimental Surgery	1991
Declared competent for the Professorship in Cardiovascular Surgery combined with position as surgeon-in-chief in The National Hospital, Oslo, Norway	1995
Professor of Cardiothoracic Surgery, University of Lund	1997

MEDICAL EXPERIENCE

Intern: Intensive Care Medicine, 1 month, 1971, Haukeland University Hospital, Norway.

Intern: Plastic and Reconstructive Surgery, 1 month, 1971, Haukeland University Hospital, Norway.

Intern: Surgery, 1 month, 1972, Nordfjord County Hospital, Norway.

Intern: Internal Medicine, 6 months, 1974, Stavanger County Hospital, Norway.

Intern: Surgery, 6 months, 1975, Stavanger County Hospital, Norway.

Intern: General Medicine, 6 months, 1975, Ramnes, Norway.

Research fellow: Department of Experimental Surgery, 6 months, 1976, The National Hospital, Oslo, Norway.

Resident in General Surgery, 3 years, 1976 -1979, Köping County Hospital, Sweden.

Chief, Medical and Surgical Services, 3 months, 1978, Troms Military Hospital, Norway.

Resident in Anesthesiology, 6 months, 1979, Köping County Hospital, Sweden.

Resident in Gynecology and Obstetrics, 1 month, 1979, Köping County Hospital, Sweden.

Senior Resident in General Surgery, 1 year, 1980, Västerås County Hospital, Sweden.

Chief, Monga Health Centre, 3 months, 1980, Monga, Zaire.

Resident in Vascular Surgery, 3 years, 1981 - 1984, Department of Surgery, University Hospital of Lund, Sweden.

Resident, Department of Pathology, 1 1/2 months, 1982, University Hospital of Lund, Sweden.

Consultant in Surgery, 1 year, 1984 - 1985, Department of Surgery, University Hospital of Lund, Sweden.

Chief, Monga Health Centre, 3 months, 1986, Monga, Zaire.

Resident in Cardiothoracic Surgery, 3 years, 1985 -1988, Department of Cardiothoracic Surgery, University Hospital of Lund, Sweden.

Chief, Monga Health Centre, 3 months, 1988, Monga, Zaire.

Consultant in Cardiothoracic Surgery, University Hospital of Lund, Sweden, since 1988.

Chief, Cardiothoracic Experimental Laboratory at the Department of Experimental Surgery, Experimental Research Center, University Hospital of Lund, since 1985.

Responsible for the clinical lung transplantation program, Department of Cardiothoracic Surgery, University Hospital of Lund, Sweden, since 1994.

Professor of Cardiothoracic Surgery, University Hospital of Lund, 1997.

A SHORT SUMMARY OF STEEN'S EXPERIENCE IN SURGERY

Steen did his six-month surgical internship at Rogaland Central Hospital in 1975. During the first six months of 1976, he worked at the Department of Experimental Surgery at the National University Hospital, Oslo. In the summer of 1976 Steen started working at the Surgical Department of Köping County Hospital, Sweden. At that time, Köping had 70 beds for surgical patients and a so-called mixed surgical ward, with responsibility for general surgery as well as orthopedics and urology. In the summer of 1977 Steen was declared competent to be second call ("bakjour"), after a letter from Dr Bergfeldt to the hospital director (see copy). Military service was completed at Troms Military Hospital in 1978 in ten months of compensatory leave saved from call duty. During the last three months of service, Steen led the medical activity at this hospital (see copy of testimonial). In 1980, Steen worked

for one year at Västerås Central Hospital, completing his residency in general surgery, and received his Swedish specialist qualification in general surgery in 1981. In January 1981, Steen started his service at the University Hospital in Lund. He worked there on the vascular surgery team and trained to be a vascular surgeon (see testimonial by the head of the vascular surgery team, Lars Norgren). From April 1984 to April 1985, Steen worked with hepatic surgery at the same clinic: during the last six months as leader for the porta team. In the spring of 1984, Steen was sent by Professor Bengmark to **Thomas Starzl** in Pittsburgh, USA. After this visit, Steen set up a liver transplantation model with pigs in Lund. This with clinical liver transplantation in mind, a plan which did not materialize, however, due to centralization of this activity to Sahlgrenska and Huddinge Hospitals. In April 1985, training in cardiothoracic surgery was initiated, and in 1988 Steen became specialist in cardiothoracic surgery. Steen's main aim and direction in this branch was adult heart surgery, and special interests were heart and lung transplantations as well as artificial hearts and lungs (see testimonials by Kugelberg, Hambraeus and Solem).

On compensatory leave, Steen worked for three periods of three months each (in 1980, 1986 and 1988) in Monga, Zaire, with the building up of a jungle hospital. Steen carried out extensive work in general surgery there, which is described in Lena Steen's special work.

Since 1991, Steen has been senior consultant (överläkare) at the Department of Cardiothoracic Surgery in Lund, which entails full clinical duty on Mondays, Tuesdays and Wednesdays. On Thursdays, Fridays and Saturdays, surgical experiments are carried out in the research laboratory built up by Steen (see testimonial by Kugelberg). In 1994 Steen became responsible for the clinical lung transplantation program at the clinic, and in 1997 Steen became professor of Cardiothoracic Surgery at the University of Lund.

FACULTY OPPONENT IN DOCTORAL DISSERTATIONS

Stig Steen has been the faculty opponent at the following doctoral dissertations:

Lars Bengtsson's doctoral dissertation at the Royal Caroline Institute, Stockholm, 1992. -Title of the thesis: "Lining of cardiovascular prosthetic materials with cultured adult human endothelium."

Guro Valen's doctoral dissertation, Tromsø University, 1994. Title of the thesis: "Cardiac injury induced by ischemia-reperfusion or toxic oxygen metabolites. Some bioactive substances as potential markers of injury."

Lars Wiklund's doctoral dissertation, University of Gothenburg, 1994. Title of the thesis: "Heart preservation for transplantation".

Øystein Bjørtuft´s doctoral dissertation, University of Olso, Norway, 1999. Title of the thesis: "Single lung transplantation, Surveillance and functional outcome".

1.

SCIENTIFIC PAPERS - STIG STEEN

The bibliography has been arranged chronologically and coded according to the following disposition.

A[1]. Original scientific papers published or accepted for publication in international journals with referee service.

B. Other scientific papers with original contents.

C. Reviews, book chapters, synopses, etc.

D. Popular science papers for the general public.

E. Short papers with original content published in scientific journals but not elsewhere.

F. Short communications published in scientific journals but also published under A.

G. Other types of publications.

[1]. *Stig Steen has been tutor for the following PhDs (the original papers in the respective theses have been marked with Roman numerals in the bibliography in accordance with the following list:*

I. "Autotransfusion. A new system." Doctoral dissertation of Jan Otto Solem MD, 14th June 1986, University of Lund, Sweden.

II. "Pneumatic antishock garments and intra-abdominal bleeding." Doctoral dissertation of Thomas Åberg MD, 18th May 1989, University of Lund, Sweden.

III. "Contraction-mediating receptors in human peripheral vessels with special reference to veins and lymphatics." Doctoral dissertation of Trygve Sjöberg, May 22, 1989, University of Lund, Sweden. Awarded the Professor Petrén prize.

IV. "ECMO- Safety & Efficacy." Doctoral dissertation of Bansi Koul MD, May 23, 1991, University of Lund, Sweden.

V. "Treatment of Critical Respiratory Failure." Doctoral dissertation of Torbjörn Wetterberg MD, December 19, 1992, University of Lund, Sweden. Awarded the Professor Eric Nilsson prize.

VI. "Preservation of Lungs for Transplantation." Doctoral dissertation of Per Ola Kimblad MD, December 18, 1993, University of Lund, Sweden.

VII. "Transplantation of Arteries." Doctoral dissertation of Giorgio Massa MD, June 11, 1994, University of Lund, Sweden.

VIII. "Preservation of the vasculature for transplantation." Doctoral dissertation of Richard Ingemansson MD, December 15, 1995, University of Lund, Sweden.

IX. "Endothelial function during ischemia-reperfusion and inhalation of nitric oxide." Doctoral dissertation of Lars Lindberg MD, December 6, 1996, University of Lund, Sweden.

X "Lung Transplantation - Clinical and experimental studies" Doctoral dissertation of Leif Eriksson MD, Marsh 20, 1998, University of Lund, Sweden.

At present, Steen is tutor for 7 doctors who plan to complete their PhD-theses according to the following plan:

	Name	Department	Topic	Schedule for dissertation
XI.	Roger Roscher, MD	Anesthesiology	Inotropics and hypothermia	1999
XII.	Algimantas Budrikis, MD	Thoracic Surgery, Kaunas University, Lithuania	New cardioplegic techniques	2000
XIII.	Ramunas Bolys, MD	Surgery, Kaunas University, Lithuania	Cadaver donor lungs	2000

XIV.	Gabriella Palmgren, MD	Anesthesiology	Platelet function after ECC and hypothermia	2001
XV.	Qiuming Liao, MD	Thoracic Surgery, Henan Medical University, Zhengzhou, China	Xenotransplantation	2002
XVI.	Per Wierup, MD	Cardiothoracic Surgery	Lung Transplantation	2000
XVII.	Johan Nilsson, MD	Cardiothoracic Surgery	Heart Transplantation	2001

Stig Steen has also been the tutor for:

XVIII. "The effects of perfusion of liver with noradrenaline on haemorrhage at experimental liver trauma in normal and cirrhotic rats. - Characterization of postjunctional α-adrenoceptors in pig hepatic, pig cystic and human cystic arteries." Master's Degree of Medical Science, by Costas Vagianos, November 4, 1986, University of Lund, Sweden.

XIX. "Monga Health Center: A vision of love." Examination work at Spyken High School in Lund, by Lena Steen, 1992.

XX. "Quality of life of lung transplant recipients. An interview study." Supplementary study programme. Advanced studies in Physical Therapy, by Margareta Sjögren, University of Lund, 1995.

XXI "A new device for cardiopulmonary resuscitation." Nynke van Cruijsen, Dpt of Experimental Thoracic Surgery, University Hospital of Groningen, The Netherlands. February 1998

PAPERS

1	A	Semb B K H, Steen S, Solhaug J H: Effect of vasopressin on canine gastric mucosal circulation. Scand J Gastroenterol 1982;17:843-848.
2	E	Steen S, Nilsson Ehle P, Norgren L, Stubbe I: Lipoproteinmönster hos claudicanter. Svensk Kirurgi 1982;40:81.
3	E	Steen S, Sjöberg T, Jönsson P-E: A new experimental model for juxtahepatic venous injuries in combination with a technique of repair including total vascular isolation and hypothermic organ perfusion. Acta Chir Scand 1983;Suppl 516:25
4	E	Steen S, Andersson L, Holmin T, Löwenhielm P, Sjöberg T, Stridbeck H, Walther B: Resorberbar eller icke resorberbar sutur vid kärlanastomos? Svensk Kirurgi 1983;41:115
5	C	Steen S, Nilsson-Ehle P: Lipoproteinmönster hos claudicanter. In: Perifer artärsjukdom. Eds: Norgren L, Persson G. Pfizer, 1983;36
6	A	Steen S, Andersson L, Lowenhielm H, Stridbeck H, Walther B, Holmin T: Comparison between absorbable and nonabsorbable monofilament sutures for end-to-end arterial anastomoses in growing pigs. Surgery 1984;95:202-207.
7	B	Steen S: Human vascular α -adrenoceptors. A study of peripheral arteries and veins in vitro and in vivo. Thesis. Bulletin no 47, Department of Surgery, Lund University, Lund, Sweden, 1984. Awarded the Professor Petrén prize, 1984.
8	A	Steen S, Skärby T V C, Norgren L, Andersson K-E: Pharmacological characterization of postjunctional α-adrenoceptors in isolated human omental arteries and veins. Acta Physiol Scand 1984;120:109-116.
9	A	Steen S, Sjöberg T, Skärby T V C, Norgren L, Andersson K-E: Postjunctional α_1- and α_2-adrenoceptors mediating contraction in isolated human groin arteries and veins. Acta Physiol Scand 1984;122:323-329.
10	A	Steen S, Sjöberg T, Skärby T, Norgren L, Andersson K-E: The postjunctional α-adrenoceptors of the human saphenous vein. Acta Pharmacol et Toxicol 1984;55:351-357.

11 E Ribbe E, Holmin T, Steen S, Thörne J: PTFE-Grafts as arterial substitutes in the infrarenal rat aorta.
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12 A Christenson J T, Norgren L, Ribbe E, Steen S, Thörne J: A ruptured aortic aneurysm that "spontaneously healed".
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13 E Pärsson H, Andersson R, Norgren L, Ribbe E, Steen S: Goretex^{R} eller Impra^{R} Graft vid femoropopliteal bypass?
Svensk kirurgi 1984;42:117.

14 F Steen S: Human Vascular α-adrenoceptors.
Svensk kirurgi 1984;42:98.

15 A Edvinsson L, Håkansson R, Steen S, Sundler F, Uddman R, Wahlestedt C: Innervation of human omental arteries and veins and vasomotor responses to noradrenaline, neuropeptide Y, substance P and vasoactive intestinal peptide.
Regul Peptides 1985;12:67-79.

16 A Steen S, Castenfors J, Sjöberg T, Skärby T, Andersson K-E, Norgren L: Effects of α-adrenoceptor subtype-selective antagonists on the human saphenous vein in vivo.
Acta Physiol Scand 1986;126:15-19.

17 A Norgren L, Elmér O, Lantz L, Steen S: Changes in intramuscular pressure in the leg during surgery. A study of a possible mechanical factor for the development of deep vein thrombosis.
VASA 1986;15:43-46.

18 E Walther B, Giorgiev K, Holmin T, Steen S, Uvelius B, Öberg S: Manuell eller maskinell sutur vid esophagustranssektion.
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19 F Åberg T, Bengmark S, Norgren L, Steen S: Intraabdominell blödning och antichockbyxor - en experimentell studie.
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20 E Berggren U, Pärsson H, Ameklo-Nobin B, Norgren L, Qvarfordt P, Ribbe E, Steen S, Thörne J: Tio års aortakirurgi, förändringar i teknik och resultat.
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21 E Sjöberg T, Alm P, Andersson K-E, Norgren L, Steen S: Perifer lymfkärlsfunktion studerad in vitro.
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22 II A Åberg T, Steen S, al Othman K, Norgren L, Bengmark S: The effect of pneumatic antishock garments in the treatment of lethal combined hepatic and caval injuries in rats.
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23 F Sjöberg T, Steen S, Andersson K-E, Norgren L: In vitro studies of human leg lymph vessels.
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24 C Sjöberg T, Steen S, Andersson K-E, Norgren L: In vitro studies of human leg lymph vessels.
In: What is New in Angiography? Eds: Maurer PC, Becker HM, Heidrich H, Hoffmann G, Kriesmann A, Müller-Wiefel H, Prätorius C. W Zuckschwerdt Verlag, Munich. 1986:120-121.

25 I A Solem JO, Steen S, Olin C: A new method for autotransfusion of shed blood.
Acta Chir Scand 1986;152:421-425.

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Enclosure 2

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